REMARKS

With the above amendments, claims 1 and 2 have been amended and claims 7-10 have been added. Claims 1-10 are pending and ready for further action on the merits. No new matter has been added by way of the above amendments. Claims 1 and 2 have been amended to insert "isolated" and claim 2 has been amended by omitting a member from the Markush group. Claims 7-10 have support in original claims 1 and 2. Reconsideration is respectfully requested in light of the following remarks.

Rejections under 35 USC §112, first paragraph

Claims 1-6 are rejected under 35 USC §112, first paragraph as allegedly not being enabled.

Applicants traverse.

Applicants submit that one of skill in the art could make and use the invention commensurate in scope with the claimed invention without undue experimentation.

The Examiner asserts that Applicants are not enabled for claims directed to a method of preventing cancer but are only enabled for claims directed to a method of reducing the occurrence of cancer. Applicants have added claims directed to the subject matter that the Examiner acknowledges is enabled (please note claims 7-10). However, Applicants assert that claims directed to a method of preventing cancer are also enabled. The Examiner states:

> *To be enabled for prevention, applicant must show that the composition comprising the ginsenosides are able to prevent cancer in each and every possible occurrence of the cancer.*

Applicants respectfully point out that the Examiner by this statement attempts to place the burden on Applicants to show that ginsenosides are able to prevent each and every possible occurrence of cancer. Applicants respectfully point out that the initial burden is not on Applicants but is rather on the Examiner to show why the claims are not enabled for their full scope. Thus, Applicants submit that the Examiner has failed to meet the burden of presenting a *prima facie* case as to why the claims would not be enabled and has failed to shift the burden to Applicants. Section 2164.04 of the MPEP citing *In re Marzocchi*, 169 USPQ 367, 370 (CCPA 1971), states:

> *It is incumbent upon the Patent Office, whenever a rejection on this basis (enablement) is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement.*

The Examiner has failed to meet this initial burden. Even if the Examiner had met this burden, Applicants have provided examples that work to prevent cancer. Absent some evidence from the Examiner that these ginsenosides would not work, one must assume that the full scope of the claimed invention is enabled by the specification.

Moreover, one of the references cited by the Examiner in the Office Action (Yun et al. Cancer Epidemiology, Vol. 4, pp. 401-408, (1995)) is entitled "Preventive Effect of Ginseng Intake against Various Human Cancers: A Case-Control Study on 1987 Pairs". Applicants point out that this is a peer reviewed article wherein the peers did not object to the phrase in the title "Preventive Effect" and thus, Applicants submit that it is recognized in the art that cancer can, to some extent, be prevented.

The Examiner also asserts that Applicants' claims are not considered to be enabled for preventing or reducing the occurrence of cancer. Applicants respectfully disagree. Regarding reducing the occurrence of cancer, Applicants note that in Table 6 on page 15 of the written description, Applicants tested female and male mice that were given doses of benzo(a)pyrene and mice that were given benzo(a)pyrene with either ginsenoside Rg_3, Rg_5, Rh_1 or Rh_2. In all cases, the incidence of cancer decreased in a statistically significant amount. These results are explained in detail on page 13, line 26 et seq. of the written description. Thus, Applicants assert that the claims are enabled at least for reducing the occurrence of cancer.

The Examiner also asserts that it is well known in the art that animal models are not considered to be enabling for human treatment. Applicants respectfully disagree and point out that the Examiner has failed to provide any evidence showing this supposed

lack of correlation. The art cited by the Examiner fails to support this supposition by the Examiner. As a matter of fact, the only art that remotely mentions a correlation indicates that the metastasis model that they use on their rats is very similar to metastasis in humans (see Iishi et al., Clin. Exp. Metastasis, 15(6), pp. 603-611, (1997)). Please see from the last sentence in the right hand column of page 603 to the first complete sentence on page 604. Applicants note that there is a difference between metastasis and preventing cancer, but simply cite the above remarks to show that there are correlations known between animal models and treating humans. Absent some evidence from the Examiner that there is no correlation, one can only assume that correlations are known to exist.

Moreover, the Examiner asserts that the prior art only shows that ginsenosides are able to treat cancer either *in vitro* or in animal models (see the first full sentence on page 4 of the Office Action). Applicants respectfully point out that there are art recognized differences between treating cancer and preventing cancer. The composition of the present invention is concerned with preventing cancer occurrence. It is well-recognized that cancer preventive action is quite different from cancer treatment action both medically and scientifically.

There have been no reports that cancer chemotherapeutics used to treat cancer can also prevent the occurrence of cancer. On the

contrary, it has been reported that a large number of cancer chemotherapeutics cause drastic disturbances on hemopoietic organs, digestive organs and/or mucous tissues.

Applicants have found that 49 kinds of cancer chemotherapeutics are used in clinic now. These are:

1) Alkylating agents : 10 kinds,

2) Nitrosoureas : 3 kinds,

3) Antimetabolites : 10 kinds,

4) Mitotic inhibitors : 9 kinds,

5) Antitumor antibiotics : 9 kinds,

6) Miscellaneous cancer chemotherapeutics : 9 kinds,

7) Combination chemotherapy : 1 kind.

Moreover, cancer chemopreventives and cancer chemotherapeutics have differences in their desired outcomes. These are summarized in the below tables.

Final goals for development of cancer chemopreventives and chemotherapeutics

Cancer chemopreventives	Cancer chemotherapeutics
- Inhibition of carcinogenesis 1. suppress cancer initiation 2. suppress cancer promotion 3. suppress malignant trans-formation	- Cancer cell death - Improvement of 5 year survival rates

Differences between the cancer chemopreventives and cancer chemotherapeutics

Cancer chemopreventives	Cancer chemotherapeutics
- Reduction of cancer occurrence or cancer prevention - Reduction of cancer deaths - Prevention of precancerous change - Prevention of precancerous lesions in high risk population - Reversal of precancerous lesions - Retardation of carcinogenesis - Improvement of cancer causing lesions	- Reduction of size or loss of cancer mass caused by cancer cell death - Prolongation of recurrence or Prevention of recurrence - Prolongation of patient survival time

Accordingly, those of skill in the art do realize that there is a difference between the treatment of cancer and the prevention of cancer (as claimed in the instant claims).

Thus, for all of the above reasons, Applicants submit that the claims are enabled. The rejection is inapposite. Withdrawal of the rejection is warranted and respectfully requested.

Rejections under 35 USC §102

Claims 1-6 are rejected under 35 USC §102(b) as being anticipated by Yun et al. (Cancer Epidemiology, Vol. 4, pp. 401-408, (1995)).

Applicants traverse.

Yun et al. do not disclose any experimental results showing the prevention of cancer. Yun et al. rather present an epidimeological study that shows that when a person takes ginseng orally, the epidemiological data shows that cancer occurrence is relatively low and there is a reduction in the risk of cancer occurrence. Moreover, Yun et al. do not report which substance of ginseng is an effective cancer chemopreventive. In ginseng, there are many substances such as phenolic compounds, polyacetylenes, sesquiterpenes, sesquiterpene alcohols, pyrazins, polysaccharides, proteins, peptides, alkaloides, amino acids, lignans, minerals and other ginsenosides in addition to the ginsenosides Rg_3, Rg_5 and Rh_2 in ginseng. The inventors have found that gisenosides Rg_3, Rg_5 and Rh_2 are isolates that are responsible for strong preventive action against cancer occurrence. These compounds were found and isolated from the many components present in ginseng, including the 40 kinds of gisenosides.

The 40 kinds of known ginsenosides in ginseng include:

1) protopanaxadiol saponin (27 kinds)

gisenosides Ra, Ra_1, Ra_2, Ra_3, Rb_1, Rb_2, Rc, Rd, Rk_1, Rk_2, Rk_3, Rs_1, Rs_2, Rs_3, Rs_4, Rs_5, Rs_7, $Rg_3(S)$, malonyl-ginsenoside Rb_1, Rb_2, Rc, Rd, quinquenoside R_1, and notoginsenoside R_4,

2) protopanaxatriol saponin (11 kinds)

ginsenosides Rf_2, Rg_1, $Rg_2(S)$, $Rg_2(R)$, $Rh_1(S)$, $Rh_1(R)$, Rh_4, F_4, 20-Glc-ginsenoside Rf, and notoginsenoside R_1, and

3) Oleanolic acid saponin (1 kind)

ginsenoside R_0.

Thus, because Yun et al. do not disclose or suggest what compounds might be effective in preventing cancer, Yun et al. cannot anticipate the instant invention. Moreover, Applicants draw the Examiner's attention to page 406, right hand column, lines 53-54 in Yun et al. wherein it is stated:

> *It is still unknown what components of ginseng work in reducing cancer risk.*

Thus, it should be apparent to those of ordinary skill in the art that prior to the instant invention it was unknown what components in ginseng could be used to reduce cancer risk, let alone those components that could be used to prevent cancer. For these reasons, the rejection is inapposite. Withdrawal of the rejection is warranted and respectfully requested.

Rejections under 35 USC §103

Claims 1-5 are rejected under 35 USC §103(a) as being unpatentable over Yun et al.

Yun et al. cannot render obvious the instant invention because Yun et al. do not disclose all of the elements of the instant

invention. As described above, Yun et al. disclose a epidemeological study that noticed the reduced incidence of cancer. Yun et al. do not disclose a method of preventing cancer. Accordingly, Applicants assert that the Examiner has failed to make out a *prima facie* case of obviousness with regard to the 35 USC §103(a) rejection over Yun et al. Three criteria must be met to make out a *prima facie* case of obviousness.

1) There must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings.
2) There must be a reasonable expectation of success.
3) The prior art reference (or references when combined) must teach or suggest all the claim limitations.

See MPEP §2142 and *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991). In particular, the Examiner has failed to meet the third element to make a *prima facie* obviousness rejection. Yun et al. do not disclose a method of preventing cancer.

Moreover, a proper *prima facie* case of obviousness has not been made because Yun et al. do not disclose or suggest that ginsenosides may be the active ingredient to prevent cancer. For these reasons, Applicants submit that the rejection has been obviated. Withdrawal of the rejection is warranted and respectfully requested.

With the above remarks and amendments, it is believed that the claims, as they now stand, define patentable subject matter such that passage of the instant invention to allowance is warranted. A Notice to that effect is earnestly solicited.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact T. Benjamin Schroeder (Reg. No. 50,990) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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